DOCKET NO.: ISIS0171-100 (ISPH-0794) **PATENT**

In the Claims:

The current status of all claims is listed below and supercedes all previous lists of claims.

1-16. (*cancelled*).

17. (*currently amended*) A method of selecting an effective antisense oligonucleotide sequence for inhibition of expression of a preselected target nucleic acid comprising:

providing a set of antisense oligonucleotide sequences 12 to 25 nucleotides in length which are complementary to a preselected target nucleic acid sequence;

selecting an antisense oligonucleotide sequence from a set of antisense oligonucleotide sequences, wherein the selected antisense oligonucleotide sequence comprises at least one activity-enhancing 5'-CCAC-3' ~~oligonucleotide~~ sequence motif ~~selected from 5' CCAC 3', 5' CCA 3', 5' TCCC 3', 5' CCCA 3', 5' CCCT 3', 5' CCCC 3', 5' ACTC 3', 5' ATCC 3', 5' CACC 3', 5' GCCA 3', 5' ATC 3', 5' CAC 3', 5' CTC 3', 5' GCAT 3', 5' ACCA 3', 5' CATC 3', 5' TCC 3', 5' AAC 3', or 5' CTCT 3'~~; and

no activity-decreasing 5'-GGGG-3' sequence motifs ~~selected from 5' GGGG 3', 5' GGG 3', 5' GGCT 3', 5' TAAA 3', 5' ACTG 3', 5' GAAA 3', 5' TGGG 3', 5' AAAT 3', 5' GGA 3', 5' CTGG 3', 5' ATAA 3', 5' AATA 3', 5' CCGG 3', 5' ATA 3', 5' GGAG 3', 5' CTG 3', 5' AAA 3' or 5' AAA 3'~~.

Claims 18 - 31 (*cancelled*)

32. (*Withdrawn*) An antisense oligonucleotide produced by the method of claim 17.

33. (*Withdrawn*) An antisense oligonucleotide of claim 32, wherein said antisense oligonucleotide is chimeric.

34. (*Withdrawn*) An antisense oligonucleotide of claim 34, wherein said oligonucleotide comprises a 2'-methoxyethyl nucleoside modification.

35. (*Withdrawn*) An antisense oligonucleotide 12 to 25 nucleotides in length targeted to a preselected target RNA, comprising:

at least one 2'modified nucleoside; and

at least two activity-enhancing sequence motifs selected from 5'-CCAC-3', 5'-CCA-3', 5'-TCCC-3', 5'-CCCA-3', 5'-CCCT-3', 5'-CCCC-3', 5'-ACTC-3', 5'-ATCC-3', 5'-CACC-3', 5'-GCCA-3', 5'-ATC-3', 5'-CAC-3', 5'-CTC-3', 5'-GCAT-3', 5'-ACCA-3', 5'-CATC-3', 5'-TCC-3', 5'-AAC-3', or 5'-CTCT-3'.

36. (*Withdrawn*) An antisense oligonucleotide of claim 35, further having no activity-decreasing sequence motifs selected from 5'-GGGG-3', 5'-GGG-3', 5'-GGCT-3', 5'-TAAA-3', 5'-ACTG-3', 5'-GAAA-3', 5'-TGGG-3', 5'-AAAT-3', 5'-GGA-3', 5'-CTGG-3', 5'-ATAA-3', 5'-AATA-3', 5'-CCGG-3', 5'-ATA-3', 5'-GGAG-3', 5'-CTG-3', or 5'-AAA-3'.

37. (*Withdrawn*) An antisense oligonucleotide of claim 35, wherein said antisense oligonucleotide is chimeric.

38. (*Withdrawn*) An antisense oligonucleotide of claim 35, wherein said oligonucleotide comprises a 2'-methoxyethyl nucleoside modification.

39. (*new*) The method of claim 17, further comprising synthesizing test antisense oligonucleotides having said antisense oligonucleotide sequences.

40. (*new*) The method of claim 39, wherein said test oligonucleotides are chimeric oligonucleotides.

41. (*new*) The method of claim 40, wherein the test oligonucleotides each have at least one 2'-subsituted nucleotide.

42. (*new*) The method of claim 39, further comprising testing the test oligonucleotides in vitro for their ability to modulate the preselected target nucleic acid.